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RISK OF PERIPHERAL ARTERIAL DISEASE (PAD) DEVELOPMENT BY MEASURING ANKLE BRACHIAL INDEX (ABI) IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Peripheral arterial disease (PAD) generally occurs as a result of progressive narrowing of arteries within the lower extremities and is a manifestation of systemic atherosclerosis. We define PAD with the aid of using the dimension ankle-brachial index (ABI) which is the most accurate tool and determination of ABI is a simple non-invasive procedure that can be easily performed on an outpatient basis. The cut-off point for diagnosis of peripheral arterial disease (PAD) & cardiovascular risk is ABI $\leq$ 0.90 or $\geq$ 1.30.

Materials and Methods: This cross sectional study involves 47 newly diagnosed hypertensive patients of age between 30-50 years. Anthropometric measurements and ABI of all the patients were done in the research lab of the Physiology department. The ABI measurements were performed by using an automated oscillometric device (Watch BP Office, Microlife, Widnau, Switzerland). In this procedure, the blood pressure was measured simultaneously on both arms followed by both ankles in the supine position.

Results: In our study out of 47 patients, 31 (66.0%) were male and 16 (34.0%) were female of mean age 43.79±6.82 years. The prevalence of deranged ABI in the present study was 10.64% according to Right ABI, while it was 6.38% according to Left ABI. A significant correlation was found for ABI in the Right ankle with SBP in the right upper limb (P=0.013) & both right and left lower limb (P<0.001 & P=0.028 respectively), while a significant correlation was also found for Left ABI with SBP in both right and left upper limbs (P=0.007 & P=0.003 respectively). We also found that 29.8% of the subjects have a low normal value of ABI (i.e., between 0.9-1.1), this is significant, even in asymptomatic patients, for Peripheral Arterial Disease (PAD).

Conclusion: So we can conclude that in newly diagnosed hypertensive patients, ABI are valuable tools for early detection of cardiovascular damage. By identifying subclinical changes before symptoms arise, healthcare providers can implement early, targeted interventions to manage hypertension more effectively and reduce the risk of long-term complications.

Keywords: Ankle brachial index, newly diagnosed hypertensive patients, peripheral arterial disease.

INTRODUCTION

Hypertension is defined by the sustained elevation of blood pressure (BP) within the systemic arteries.[1] Blood pressure is conventionally represented as the ratio between systolic BP (the force exerted by blood on arterial walls during heart contraction) and diastolic BP (the pressure when the heart is at rest).[1,2,3]

Hypertension can stem from various causes; however, the most common factor in approximately 90% to 95% of the patients is complex and a combination of genetic and environmental factors.[4] A notable number of individuals with hypertension have a positive family history, and studies suggest that heritability, representing the influence of genetic factors, ranges between 35% and 50% in most cases.[4,5] Many studies have reported that nearly 120 loci are associated with BP regulation and together explain 3.5% of the trait variance.[6,7] Such findings suggest the importance of search for new pathways and new biomarkers for the development of more modern omics-driven diagnostic and therapeutic modalities for hypertension in the era of precision medicine.[8,9,10]

In terms of the burden of the disease, where on one hand hypertension along with diabetes is known to cause significant mortality,[11] on the other hand, hypertension exerts immense pressure on patient and the healthcare system alike, financially. Epidemiological studies aimed at determining the causes of hypertension suggest two main risk factors namely, increased weight or obesity.[12,13,14]

Hypertension is not only a chronic disease, but is often accompanied by the disorders of the peripheral nervous system.[15,16]

Important tool that has been found to be effective in evaluating vascular function is the Ankle-Brachial Index (ABI). ABI is also a non-invasive tool for the assessment of vascular status. ABI is essentially a ratio between the systolic blood pressure at the ankle, and the systolic blood pressure of either of the upper limb, whichever is higher.[17,18] Since, the ratio compares the resistance of the blood vessels, and is based on the fact that the diameter of vessels should only vary as a stimulus to a variety of internal factors or external factors.[19,20]

MATERIAL AND METHODS

Subjects

The present study was an Observational, Cross-sectional study. This study began only after ethical clearance was obtained from the institutional ethical committee of DR. RMLIMS, Lucknow (Ref no. RC-483/RMLIMS/2022/IEC No. 73/22).

A total 47 newly diagnosed hypertensive patients were recruited in this study from the general medicine OPD of DR. RMLIMS, Lucknow. An informed consent was taken on the prescribed consent form from each participant who agreed to participate in this study; the form was obtained from the research cell of the institute. Then Anthropometric measurement and ABI of all the patients (who fulfilled the inclusion and exclusion criteria of the study) were done in the research lab of the Physiology Department.

Inclusion criteria- Age of patients were between 30 to 50 years, newly diagnosed Hypertensive Patients without any antihypertensive medications and Patients of both sexes are involved in study.

Exclusion Criteria include- Diabetic patients, Patients with long-standing hypertension, chronic alcoholics, chronic smokers, Patients with a past history of cerebrovascular accidents, Patients with peripheral nervous system disorder and patients having history of Hypothyroidism/Hyperthyroidism.

Procedures

Anthropometric measurements of all patients were done in the research lab of department of physiology of Dr. RMLIMS, Lucknow, following a standard protocol. Weight was measured on a calibrated balance scale with the subject wearing light clothing and no shoes. Height was measured by rigid stadiometer to the nearest centimetre while barefoot. BMI was calculated by using Quetelet index- i.e. BMI= weight/height^2 (weight was taken in kilogram and height in meters).

The measurements of ABI were performed by using an automated oscillometric device (Watch BP Office, Microlife, Widnau, Switzerland) equipped with two cuffs for simultaneous double arm BP measurements.[21,22] All the patients were given rest for at least 5 min in supine position before the measurement of blood pressure. The patients were also advised not to consume tea/coffee or any cardiomodulator substance before the test.

The blood pressure (BP) was measured while the patient lies comfortably in a supine position with the arms and legs at the same level as the heart. BP was measured simultaneously on both upper arms by applying the appropriate size cuff over the arm 2 inches above the cubital fossa, completely covering the brachial artery. After that, the ankle blood pressure was measured by applying the cuff to the ankle above the malleoli. The systolic and diastolic blood pressure (BP) was measured three times at interval of one minute. The average of the three measurements was used in the analysis.[23,24] ABI was then calculated by dividing the systolic blood pressure of each of the ankles by the highest brachial systolic blood pressure of either arm (Rt or Lt).[25]

After recording the blood pressure, cuffs were removed and the patients were allowed to leave. The blood pressure reading was noted day wise and ABI was calculated.

Data Analysis

For the data analysis, we used parametric and non-parametric test, as required. In the parametric test, normality test, t-test, spearman's correlation test was used. In the nonparametric test □2-test (chi square test) was used for the association of attributes. SPSS ver. 21 was used for the analysis. A P-value of <0.05 was considered significant.

RESULTS

In table-1, Mean age of the patients was 43.79±6.82 years. Majority of the patients were aged between 41 & 50 years. Male preponderance of 1.94 was found in the study population. Females constituted only 34%. Weight & Height ranged from 40 to 95 kg and 144 to 180 cm. Mean BMI was 25.11±4.50 kg/m2.Systolic Blood Pressure in Right Arm was 148.45±13.31 mmHg, while in Left Arm was 144.10±15.55 mmHg. Systolic Blood Pressure in Right Leg was 165.81±15.81 mmHg, while in Left Leg was 166.64±17.14 mmHg. Diastolic Blood Pressure in Right Arm was 88.47±8.11 mmHg, while in Left Arm was 88.26±8.20 mmHg. Diastolic Blood Pressure in Right Leg was 86.30±8.71 mmHg, while in Left Leg was 87.34±7.82 mmHg.

In table-2, A statistically significant correlation was found for Right ABI with Systolic BP (SBP) in Right Arm & both (right & left) lower limbs. While, only SBP of Right & Left Arm was significantly correlated with Left ABI. [Table 2]

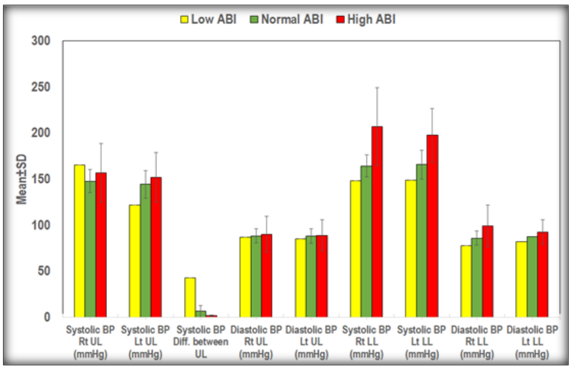

Figure 1: Association of Left ABI levels with different Blood pressure (BP) measures

In table-3, Among patients with High ABI (>1.3) higher BP was found at all limbs and across the laterality, while Difference (diff.) in upper limb (UL) SBP was lower. On comparing statistically, a significant difference was found in diff. in UL SBP, and SBP in lower limbs (LL) (both Right & Left) among patients with different levels of ABI. [Table 3]

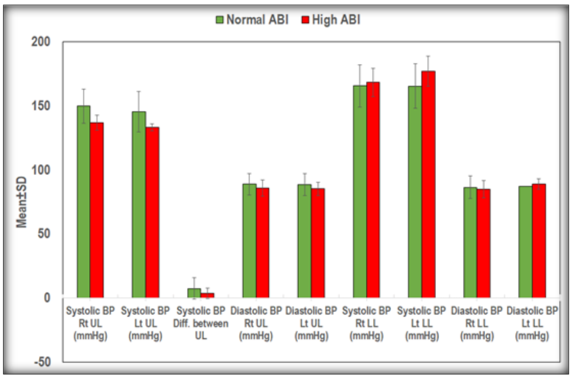

Figure 2: Association of Right ABI levels with different Blood pressure (BP) measures

In table-4, Among patients with High ABI (>1.3) higher BP was found only for SBP reading at lower limbs (both right and left) and DBP at left lower limb, while at other readings, BP was lower among High ABI patients. On comparing statistically, a significant difference was found in SBP at the right upper limb between patients with different levels of ABI. [Table 4]

In tablet 5, a considerable proportion of subjects (29.8%) have low normal ankle ABI values (0.9-1.1). [Table 5]

Table 1: Distribution of the study population (N=47)

AGE	**No. (%)**
30-40 years	15 (31.91%)
41-50 years	32 (68.1%)
GENDER	**No. (%)**
Males	16 (34.0%)
Females	31 (66.0%)
ANTHROPOMETRIC PARAMETERS	**Mean ±SD**
Weight (Kg)	65.38±11.68
Height (Cm)	161.30±8.60
BMI ($Kg/m^{2)}$	25.11±4.50
BLOOD PRESSURE (SBP and DBP in mmHg)	**Mean ±SD**
Right Upper Limb SBP	148.45±13.31
Left Upper Limb SBP	144.10±15.55
Right Lower Limb SBP	165.81±15.81
Left Lower Limbs SBP	166.64±17.14
Right Upper limb DBP	88.47±8.11
Left Upper Limb DBP	88.26±8.20
Right Lower Limb DBP	86.30±8.71
Left Lower Limb DBP	87.34±7.82
ABI Profile	**Mean ±SD**
Right ankle ABI	1.13 ± 0.10
Left ankle ABI	1.17 ± 0.14

Table 2: Correlation of ABI with Blood Pressure (BP) Parameters

		Right ABI	Left ABI
SBP Right Upper Limb (mmHg)	**'r'**	-0.361	-0.386
	'p'	0.013	0.007
SBP Left Upper Limb (mmHg)	**'r'**	-0.188	-0.422
	'p'	0.206	0.003
DBP Right Upper Limb (mmHg)	**'r'**	-0.227	-0.122
	'p'	0.125	0.415
DBP Left Upper Limb (mmHg)	**'r'**	-0.196	-0.202
	'p'	0.188	0.174
SBP Right Lower Limb (mmHg)	**'r'**	0.562	0.092
	'p'	<0.001	0.538
SBP Left Lower Limb (mmHg)	**'r'**	0.320	0.118
	'p'	0.028	0.429
DBP Right Lower Limb (mmHg)	**'r'**	0.099	0.026
	'p'	0.509	0.860
DBP Lower Left Limb (mmHg)	**'r'**	-0.048	-0.007
	'p'	0.747	0.962

Table 3: Association of Left ABI levels with different Blood pressure (BP) measures

	Low ABI (n=1)		Normal ABI (n=44)		High ABI (n=2)		ANOVA	
	Mn	**SD**	**Mn**	**SD**	**Mn**	**SD**	**F**	**'p'**
Systolic BP Rt UL (mmHg)	165.00	0.00	147.70	12.49	156.50	31.82	1.219	0.305
Systolic BP Lt UL (mmHg)	122.00	0.00	144.25	15.09	152.00	26.87	1.285	0.287
Systolic BP Diff. between UL	43.00	0.00	6.55	6.38	1.50	0.71	17.167	<0.001
Diastolic BP Rt UL (mmHg)	87.00	0.00	88.43	7.82	90.00	19.80	0.050	0.951
Diastolic BP Lt UL (mmHg)	85.00	0.00	88.30	8.06	89.00	16.97	0.084	0.920
Systolic BP Rt LL (mmHg)	148.00	0.00	164.34	11.70	207.00	42.43	10.887	<0.001
Systolic BP Lt LL (mmHg)	149.00	0.00	165.64	15.56	197.50	28.99	4.417	0.018
Diastolic BP Rt LL (mmHg)	78.00	0.00	85.91	7.73	99.00	22.63	2.841	0.069
Diastolic BP Lt LL (mmHg)	82.00	0.00	87.23	7.70	92.50	13.44	0.663	0.520

Table 4: Association of Right ABI levels with different Blood pressure (BP) measures

	Normal ABI (n=42)		High ABI (n=5)		Student's t-test	
	Mn	**SD**	**Mn**	**SD**	**'t'**	**'p'**
Systolic BP Rt UL (mmHg)	149.81	13.32	137.00	5.92	2.109	0.041
Systolic BP Lt UL (mmHg)	145.38	15.97	133.40	2.70	1.659	0.104
Systolic BP Diff. between UL	7.52	8.53	3.60	4.04	1.008	0.319
Diastolic BP Rt UL (mmHg)	88.79	8.31	85.80	6.26	0.775	0.443
Diastolic BP Lt UL (mmHg)	88.62	8.46	85.20	5.22	0.879	0.384
Systolic BP Rt LL (mmHg)	165.52	16.36	168.20	11.03	-0.354	0.725
Systolic BP Lt LL (mmHg)	165.40	17.36	177.00	11.85	-1.447	0.155
Diastolic BP Rt LL (mmHg)	86.48	8.95	84.80	6.80	0.404	0.688
Diastolic BP Lt LL (mmHg)	87.17	8.17	88.80	4.09	-0.438	0.664

Table 5: Distribution of study population according to Right Ankle ABI & Left Ankle ABI Values

Right Ankle ABI	No. of participants (%)
<0.9	0 (0%)
0.9-1.1	14 (29.8%)
1.1-1.3	28 (59.6%)
>1.3	5 (10.6%)
Left Ankle ABI	
<0.9	1 (2.1%)
0.9-1.1	14 (29.8%)
1.1-1.3	30 (63.8%)
>1.3	2 (4.3%)

DISCUSSION

By obtaining a detailed clinical history, assessment of anthropometric measures, and ABI measurements, clinicians can understand the patient's cardiovascular health comprehensively.

In terms of the age and gender distribution of the patients in the present study, the age ranged between

30 to 50 years, with a higher proportion of patients in their 4th decade of life (68.1%), mean age was 43.79±6.82. While, Males were almost twice as compared to females (66.0% vs. 34.0%). The patient`s BMIs varied from 17 to 41 kg/m2, mean BMI was 25.11±4.50. We measured the Systolic and Diastolic blood pressure across 4 limbs, Right & Left arm were selected as Upper Limbs, while the Left and Right Calves were the Lower Limbs. The systolic and diastolic blood pressures among these limbs ranged between 144.10±15.55 mmHg and 166.64±17.14 mmHg, and 86.30±8.71 mmHg and 88.47±8.11 mmHg.

Ishida et al. (2019),[26] shared lots of similarities with the present study, firstly, in their study they reported the median age of patients at high risk of developing hypertension was 51 years, which was very similar to the present study, however in terms of gender distribution, they reported a 55.0% of the study population were women.

In the present study, the ABI in left and right ankle were 1.13±0.10 and 1.17±0.14. These values fall within the normal range for ABI, which is typically 0.9 to 1.3, indicating no severe peripheral artery disease (PAD) among the participants. We also evaluated the correlation of the ABI in both ankles with the blood pressure among the limbs, a significant correlation was found for ABI in the Right ankle with SBP in the right upper limb & both right and left lower limb, while a significant correlation was also found for Left ABI with SBP in both upper limbs. This suggests that ABI can reflect arterial stiffness and blood pressure changes in specific limbs. In the present study, on categorising left ABI into Low, Normal and High and comparing the blood pressure parameters among the categories, the difference in SBP of the Upper Limb was significantly higher in patients with Low ABI, while SBP in both lower limbs was significantly higher in patients with High ABI. On the other hand, none of the patients had Low right ABI, and hence blood pressure in all limbs was compared between patients with Normal & High ABI, we found a significantly higher SBP in the right upper limb in patients with Normal ABI as compare to High ABI.

In this study, we found that 29.8% of the subjects have a low normal value of ABI (i.e., between 0.9-1.1), this is significant, even in asymptomatic patients, for Peripheral Arterial Disease (PAD). ABI values between 0.9 and 1.1 are within the normal range, but they can be indicative of a potential future risk for PAD, even if the individual is currently asymptomatic. These borderline values suggest that there may be some degree of arterial stiffening or minor narrowing that could progress over time. These subjects should be counselled on lifestyle modifications and possibly preventive measures to mitigate the risk of developing symptomatic PAD in the future.

Our study is in accordance with O'Hare et al (2006),[27] who observed that the mortality risk was higher than the reference category for participants with Ankle-Brachial Index (ABI) values above the traditional cut point of 0.9. Specifically, this increased risk was noted in participants with ABI values ranging from 0.91 to 1.0 and those with values equal to or greater than 1.4.

The findings in our study are in agreement with the study done by Alves-Cabratosa et al (2019),[28] who suggest that while high ABI values (≥1.3) are associated with increased mortality, the strength of this association is weaker compared to the high-risk group with ABI values <0.9. Nonetheless, it is important to recognize that high ABI values still pose a significant risk, similar to those with borderline-low ABI values (0.9–1.1). This implies that even in the absence of clear symptoms of PAD, patients with high ABI and borderline-low ABI should be monitored closely for cardiovascular complications, especially if they have underlying hypertension.

The present study is rather novel in all regards. While the ABI is a useful indicator of arterial stiffness, which is a crucial component of cardiovascular health and can provide early warnings about potential complications in hypertensive patients. There have been only limited studies in evaluating ABI in hypertensive patients and fewer in newly diagnosed hypertension. However, most of the contemporary studies have been done to elucidate the role of ABI in the progression of hypertension and associated risk factor.

The study's findings on Ankle Brachial Index (ABI) in newly diagnosed hypertensive patients offer valuable insights into the relationship between ABI and blood pressure, as well as the broader implications for cardiovascular health.

In the current study, the focus on newly diagnosed patients within a specific age range (30-50 years) adds valuable data to this trend, highlighting the onset of arterial changes early in the course of hypertension.

The current study is in accordance with Ishida et al. (2019),[26] who reported that ABI was lowest for participants younger than 40 years and increased with age. This suggests that arterial stiffness increases with age, a factor that could influence hypertension management strategies in different age groups.

Sun et al. (2021),[29] reported that ABI was significantly higher in patients with LVH than in those without (1.13±0.11 vs. 1.11±0.11). The findings in the current study align with this, as elevated ABI values can indicate increased arterial stiffness, often associated with hypertensive heart disease such as LVH.

Armas-Padrón et al. (2022),[30] demonstrated that patients with lower ABI (≤0.9) had higher incidences of cardiovascular disease (CVD), mortality, and hospitalizations compared to those with higher ABI (>1.4). This underscores the predictive value of ABI for severe cardiovascular outcomes. The current study's findings of normal

ABI values suggest that while newly diagnosed hypertensive patients may not yet exhibit severe arterial stiffness, monitoring ABI could help predict and prevent future CVD.

The prevalence of deranged ABI in the present study was 10.64% according to Right ABI, while it was 6.38% according to Left ABI.

Our studies finding concur with those of the study conducted by Hendriks et al. (2016),[31] they included 6538 individuals with CVD or at high risk for CVD and found that 4.5% of them had ABI ≥1.4. While Velescu et al. (2017),[32] included 5679 individuals at risk of CHD; of them, 97.1% had normal ABI; while the remaining 2.9% had abnormal ABI. These studies contextualize the normal ABI values found in the present study, indicating that newly diagnosed hypertensive patients might still be in the early stages of arterial changes.

In hypertensive patients, there is a complex interplay of reduced angiogenesis (as indicated by high endostatin and low pro-angiogenic mediators like angiogenin and bFGF) and increased inflammation (evidenced by high CRP, VEGF, and IL-8 levels). These changes may contribute to the vascular complications commonly associated with hypertension, including atherosclerosis and endothelial dysfunction.[33] Reduced levels of pro-angiogenic mediators (bFGF and angiogenin) and increased levels of endostatin, an anti-angiogenic factor, can impede vascular healing and prevent the growth of new blood vessels. This could exacerbate atherosclerosis, leading to lower ABI values and increased risk of PAD in hypertensive patients.

Limitations-

The small sample size limits the study's power and representativeness. The cross-sectional design only offers a snapshot in time, not causality. A control group was lacking, which weakens the findings. Future studies should include larger samples, a control group, and longitudinal designs to strengthen conclusions.

CONCLUSION

In our study, significant correlations were seen between the ABI in the right ankle and the SBP in the right upper limb and both lower limbs, and between the left ankle and the SBP in both upper limbs. The prevalence of deranged ABI was 10.64% according to Right ABI, while it was 6.38% according to Left ABI.

In our study, we also identified that approximately one-thirds of the newly diagnosed hypertensive patients had low normal ABI values. This finding suggests a potential future risk for PAD in individuals who are currently asymptomatic.

So we can conclude that in newly diagnosed hypertensive patients, ABI are valuable tools for early detection of cardiovascular damage. By identifying subclinical changes before symptoms arise, healthcare providers can implement early, targeted interventions to manage hypertension more effectively and reduce the risk of long-term complications. This proactive approach can improve patient outcomes and quality of life by addressing issues at a stage when they are more easily manageable.

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